

CLAIMS

1. A human anti-human interleukin-18 antibody against human interleukin-18.

2. The human anti-human interleukin-18 antibody according to Claim 1, comprising:

an H-chain complementarity determining region consisting of (a) a polypeptide consisting of amino-acid sequences represented by SEQ ID NOS: 4 to 6, or (b) a polypeptide consisting of amino-acid sequences, represented by SEQ ID NOS: 4 to 6, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as the H-chain complementarity determining region against human interleukin-18; and

an L-chain complementarity determining region consisting of (c) a polypeptide consisting of amino-acid sequences represented by SEQ ID NOS: 10 to 12, or (d) a polypeptide consisting of amino-acid sequences, represented by SEQ ID NOS: 10 to 12, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as the L-chain complementarity determining region against human interleukin-18.

3. The human anti-human interleukin-18 antibody according to Claim 1 or 2, comprising:

an H-chain variable region consisting of (e) a polypeptide consisting of an amino-acid sequence represented by SEQ ID NO: 3, or (f) a polypeptide consisting of an amino-acid sequence, represented by SEQ ID NO: 3, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as the H-chain variable region against human interleukin-18; and

an L-chain variable region consisting of (g) a polypeptide consisting of an amino-acid sequence represented by SEQ ID NO: 9, or (h) a polypeptide consisting of an amino-acid sequence, represented by SEQ ID NO: 9, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as the L-chain variable region against human interleukin-18.

4. An H-chain variable region fragment of a human-derived antibody against human interleukin-18, the fragment consisting of (e) a polypeptide consisting of an amino-acid sequence represented by SEQ ID NO: 3, or (f) a polypeptide consisting of an amino-acid sequence, represented by SEQ ID NO: 3, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as an H-chain variable region against human interleukin-18.

5. An L-chain variable region fragment of a human-derived antibody against human interleukin-18, the fragment consisting of (g) a polypeptide consisting of an amino-acid sequence represented by SEQ ID NO: 9, or (h) a polypeptide consisting of an amino-acid sequence, represented by SEQ ID NO: 9, one or more amino acids of which are substituted, deleted, inserted, and/or added, and which serves as an L-chain variable region against human interleukin-18.

6. A single-chain variable region fragment of a human-derived antibody against human interleukin-18, the fragment comprising:

(1) an H-chain variable region fragment including the H-chain complementarity determining region according to Claim 2, or (2) the H-chain variable region fragment according to

Claim 4; and

(3) an L-chain variable region fragment including the L-chain complementarity determining region according to Claim 2, or (4) the L-chain variable region fragment according to Claim 5,

the H-chain variable region fragment and the L-chain variable region fragment being ligated to each other.

7. A human-derived antibody against human interleukin-18, or a fragment thereof, the antibody or fragment comprising:

(1) an H-chain variable region fragment including the H-chain complementarity determining region according to Claim 2, or (2) the H-chain variable region fragment according to Claim 4; and/or

(3) an L-chain variable region fragment including the L-chain complementarity determining region according to Claim 2, or (4) the L-chain variable region fragment according to Claim 5,

the H-chain variable region fragment and/or the L-chain variable region fragment being ligated to a human-derived constant region.

8. The fragment according to Claim 7, which comprises an Fab fragment, an Fab' fragment, an  $F(ab')_2$  fragment, an scAb fragment, or an scFvFc fragment.

9. A modified antibody, comprising the antibody according to any one of Claims 1 to 8, or the fragment thereof, and a modification agent binding thereto.

10. A gene coding for either (1) the antibody according to

any one of Claims 1 to 8, or (2) the fragment thereof.

11. The gene according to Claim 10, comprising as an open reading frame region a base sequence represented by SEQ ID NO: 1 or 7.

12. A recombinant expression vector, comprising the gene according to Claim 10 or 11.

13. A transformant, comprising the gene according to Claim 10 or 11 introduced therein.

14. A method for producing either (1) a human-derived human anti-human interleukin-18 antibody, or (2) a fragment thereof, by causing a host to express the gene according to Claim 10 or 11.

15. A detector for interleukin-18, the detector using (1) the antibody according to any one of Claims 1 to 8, (2) the fragment thereof, or (3) the modified antibody according to Claim 9.

16. A diagnostic kit for measuring an amount of human interleukin-18 contained in a test sample, the diagnostic kit using (1) a detecting reagent including the antibody according to any one of Claims 1 to 8, (2) the fragment thereof, or (3) the modified antibody according to Claim 9.

17. A method for diagnosing immunological disease in accordance with an amount of human interleukin-18 contained in a test sample and measured by using the detecting reagent according to Claim 16.

18. A human interleukin-18 activity inhibitor, comprising a human interleukin-18 antagonist as an active ingredient.

19. The human interleukin-18 activity inhibitor according to Claim 18, wherein the human interleukin-18 antagonist is any one of following substances selected from:

- (i) the human anti-human interleukin-18 antibody according to any one of Claims 1 to 3;
- (ii) the fragment according to any one of Claims 4 to 8;
- (iii) the modified antibody according to Claim 9; and
- (iv) a low-molecular compound obtained through molecular designing in accordance with an antigen determining region on human interleukin-18, the antigen determining region being recognized by (1) the antibody according to (i), (2) the fragment according to (ii), or (3) the modified antibody according to (iii).

20. A gene therapy agent, comprising the gene according to Claim 10 or 11.

21. An immunological disease treatment agent, comprising (1) the human interleukin-18 activity inhibitor according to Claim 18 or 19, or (2) the gene therapy agent according to Claim 20.

22. A method for treating immunological disease by administering the immunological disease treatment agent according to Claim 21.

23. The immunological disease treatment agent according to Claim 21, which inhibits cytokines produced from helper T1 cells stimulated with an antigen and human interleukin-18.

24. The immunological disease treatment agent according to Claim 21 or 23, which is applied to human interleukin-18-related allergy, inflammation, and chronic immune abnormality disease.